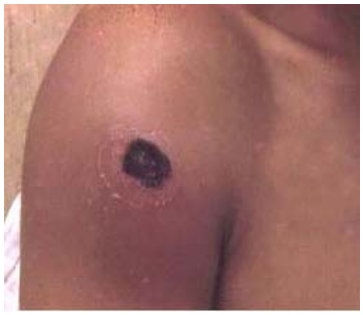
Anthrax Disease Investigation Plan

Disease and Epidemiology

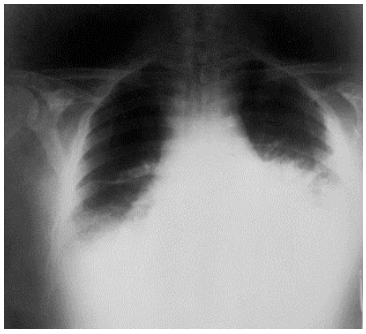
Clinical Description:

There are three clinical presentations of anthrax:

Cutaneous:
This is the most common clinical presentation. The disease creates a lesion (papular, becoming vesicular, and finally appearing as an eschar or a black depressed lesion) at the site of entry. Significant edema (swelling) surrounds the eschar. The ulcer is usually painless and typically is misdiagnosed as an insect bite or Orf (Orf is a virus that causes ulcers) until the eschar presentation.



Inhalational:
This is a rare presentation. Initial symptoms are flu-like, including fever, malaise, nausea, vomiting, and mild cough or chest pain. The disease worsens rapidly (within 3-5 days), with respiratory distress and shock. Diagnosis is typically through chest xray that shows a characteristic mediastinal widening, which is then confirmed by culture. Death is common.



Gastrointestinal:
This is also a rare presentation. It presents as abdominal distress, followed by fever, septicemia and death.

Causative Agent:

Anthrax is caused by a gram-positive spore-forming bacillus, *Bacillus anthracis*. These cells produce three virulence factors: an antiphagocytic capsule and two toxins (lethal and edema). These factors are responsible for hemorrhage, edema, and necrosis that accompany this disease.

Differential Diagnosis:

The differential diagnosis for inhalational anthrax includes pneumonia, influenza, and bronchitis. The differential diagnosis for cutaneous anthrax includes spider bites and Orf.

Laboratory Identification:

Anthrax is generally identified via culture or PCR. The organisms are easy to grow, but can be difficult to differentiate from other Bacillus species that are benign. Typically, clinical laboratories should attempt to rule out the presence of anthrax in blood cultures

and lesions within 24 hours. If anthrax cannot be ruled out, then the isolate should be forwarded immediately to the Utah Public Health Laboratory for final identification.

Samples:

Cutaneous – Collect all samples listed below on all suspect patients:

- **Swab** - Collect two separate swabs (dacron or rayon only) of the lesion (one is for Gram stain and culture, the other for PCR). DO NOT use calcium alginate or cotton swabs, as they will interfere with the PCR test. Collect vesicular fluid aseptically on dry sterile swabs from previously unopened vesicles. If lesion is an eschar, carefuly lift the eschar's outer edge and insert a sterile dry swab and rotate for 2-3 seconds, beneath the edge of the eschar.
- **Biopsy** – Collect biopsy specimens from both vesicle and eschar, if present
    - **If patient has been on antibiotics for at least 24 hours:** collect one full-thickness punch biopsy from papule or vesicle which includes adjacent skin – place into 10% buffered formalin for histopathology and immunohistochemistry.
    - **If patient is NOT on antibiotics or has only received antibiotics within the preceding 24 hours:** collect two full-thickness punch biopsies from papule or vesicle which includes adjacent skin – place ONE of the biopsies into 10% buffered formalin and the SECOND one should be fresh frozen (for culture, Gram stain, PCR, and frozen tissue IHC).
- **Serum –** Always collect an acute serum sample as soon as the diagnosis is suspected. Always collect a convalescent serum sample 14-35 days after symptom onset.

Inhalational - Collect all samples listed below on all suspect patients:

- **Blood** – Collect typical volume and number of sets for blood culture as described by your institution. Also, collect an additional 10 ml of blood (for pediatric cases, collect the volume allowable) in an EDTA tube for PCR.
- **Pleural Fluid** – Collect pleural fluid and place into a sterile container (test for culture, Gram stain, and PCR).
- **CSF** - Collect CSF if meningeal signs are present or if meningitis is suspected. (Test for culture, Gram stain, and PCR).
- **Serum** - Always collect an acute serum sample as soon as the diagnosis is suspected. Always collect a convalescent serum sample 14-35 days after symptom onset.
- **Biopsy** – If available, submit a bronchial or pleural biopsy. These should be stored and shipped BOTH as fresh frozen tissue AND as formalin fixed samples.

Gastrointentinal –

- Blood and stool samples

Information on sample size and transport are posted in the following table.

Test Types	Samples	Size (minimum)	Transport <2 hours	Transport > 2 hours	Do Not Send
Culture and PCR	Isolate	Plate/slant	RT*	RT	Broth
	Swabs[1]		RT	RT	On Transport media
	Blood, whole	1.0 ml in EDTA or Na citrate tubes	RT	2-8ºC	Blood culture bottle or heparin tube
	Fluids (pleural, bronchial, CSF)	0.5 ml	RT	2-8ºC	
	Blood clot	1.0 ml clot	RT	2-8ºC	
	Tissue, fresh	5 mm^3 in container	2-8ºC	Frozen at –79ºC	Preserved tissue
	Serum, separated and removed from clot	1.0 ml	RT	2-8ºC	Frozen serum
	Citrated plasma, separated and removed from clot	1.0 ml	RT	2-8ºC	Frozen plasma
	Stool	≥ 5 g	2-8ºC	2-8ºC	
Serology	Serum, separated and removed from clot	1.0 ml	2-8ºC	Frozen at ≤ - 20ºC	Whole blood, blood culture bottle, plasma
	Citrated plasma, separated and removed from clot	1.0 ml	2-8ºC	Frozen at ≤ - 20ºC	Plasma from EDTA or heparin
Histopathology	Tissue preserved in 10% buffered formalin	1.0 cm^3	RT	RT	Fresh or frozen tissue
	Biopsies of lesions, preserved in 10% buffered formalin	0.3 mm diameter	RT	RT	Fresh or frozen tissue

* Room Temperature
[1] From lesions

Treatment:

Anthrax treatment is typically ciprofloxacin or doxycycline. Specific guidelines can be found at the following site:
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5042a1.htm#tab1

Case Fatality:

For cutaneous, death is rare when treated properly. Without appropriate treatment death rates can range from 5-20%. Fatality rates with inhalational and gastrointestinal, even with appropriate treatment, are much higher.

Reservoir:
Anthrax spores remain viable in soil for years. Ungulates are at risk of this disease. Presence of this disease should be investigated thoroughly to determine whether it could be due to bioterrorism.

Transmission:
Anthrax is not transmitted from person to person. Transmission is generally through contact with contaminated products such as hides and meat. All cases of anthrax should be investigated though, to assure that they are not possibly due to terrorism.

Incubation Period:
Typically the incubation period is 1-7 days, although longer incubation periods (up to 40 days) are possible.

Susceptibility:
All humans are susceptible to anthrax.

Epidemiology:
There are typically no cases of anthrax occurring in Utah in recent history. Any suspect cases should be thoroughly investigated.

Public Health Control Measures
Public Health Responsibility:
- Thoroughly investigate all suspect cases of disease
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention
- Initiate active surveillance immediately upon notification of suspect cases

Prevention:
There is a vaccine available, but its use is strictly limited to:

- Persons who work directly with the organism in the laboratory.
- Persons who work with imported animal hides or furs in areas where standards are insufficient to prevent exposure to anthrax spores.
- Persons who handle potentially infected animal products in high-incidence areas; while incidence is low in the United States, veterinarians who travel to work in other countries where incidence is higher should consider being vaccinated.
- Military personnel deployed to areas with high risk for exposure to the organism.
- Post-exposure prophylaxis.

Prevention in Healthcare Settings:

Because anthrax is not transmissible from person to person (although there may be some risk of transmission from a cutaneous lesion), standard precautions are recommended. For further information please see:
http://www.cdc.gov/ncidod/dhqp/pdf/bt/13apr99APIC-CDCBioterrorism.PDF

Outbreaks:

Due to the serious nature of this disease, single cases will be investigated as soon as possible. Public health will assume that a single case could be leading to an outbreak and will react accordingly. Public health will have a large mission of public, clinician, and first responder education in the event of a real outbreak.

Isolation and Quarantine Requirements:

As this is a disease that is not typically transmitted from person to person, isolation and quarantine are generally not appropriate. An exception would be made for environmental quarantine, should a location be identified as possibly contaminated with anthrax.

Case Investigation

A. I. "White Powder Incidents" – Exposure to unknown substance

Situation: Several times per year, first responders (and local health departments) are called upon to investigate exposure to an unknown substance. If the substance is a white powder, then there is concern that the substance contains anthrax. It is unlikely that these substances will turn out to contain an agent, but the substances need to be handled with care and with the assumption that they could contain an agent.

- When a call comes in that there is a "white powder incident" or exposure to any unknown substance, the first step is to contact first responders, the local health department, UPHL, UDOH Epidemiology, and the FBI. UDOH Epidemiology should be contacted 24/7 using the 1-888-EPI-UTAH number. The on-call epidemiologist should notify the State Epidemiologist, CDEP Program Manager, and Anthrax Epidemiologist, the State Laboratory Director, and the Microbiology Bureau Director, as well as assure that the local health department (including local health officer) have been notified. The incident should be posted to the Epidemiology Issue Tracker as soon as possible. Preferably, the incident should also be posted to UNIS.
- The area should be contained and all exposed people removed from the area of exposure. Shelter in place is never an option for people exposed to an unknown substance.
- If the people are ill, suspect a chemical agent, decontaminate immediately and have them receive medical attention.
- If people are well, collect identifying information (name, address, contact phone numbers) from all individuals who were exposed. Ask them to remain in a safe, contained location until after the risk assessment.
- Do not touch or move the unknown substance. Initiate a risk assessment of the likelihood that this substance presents a threat. The FBI will assist with this risk

assessment. Sending the sample to the laboratory for testing is NOT a substitute for a thorough risk assessment.

- If the risk analysis indicates a lack of threat, notify everyone and stand down. You may release the people without restriction.
- If the risk assessment indicates a possible threat, continue with this process.
- If the people are well, ensure that they wash thoroughly with soap and water and change into clean clothing. Bag their clothing. Once identifying/contact information has been collected, people may be released without restriction. People should be encouraged to stay on site for the washing procedure, but if they wish, they can be allowed to return home to shower.
- Optimally, the unknown substance should not be touched or moved before it is analyzed for the presence of radiologic, chemical, or explosive agents. Packaging and transporting an unknown substance is risky and may injure the transporting parties. Work with CSTE, EMS, and the FBI to conduct this testing prior to transport.
- If you must move the sample for radiologic, chemical, and explosive agent analysis, then the sample must be packaged in a way to minimize exposure of the transporting individuals. Do not take a sample to the UPHL lab until the sample has been documented that radiological, chemical, and explosives testing has occurred and the sample is negative for all three.
- When the sample arrives at UPHL, be prepared to list possible agents for testing. The listing of agents should come from the risk assessment. There is no reason to believe that a "white powder" is more likely to contain anthrax than any other biological agent. Ruling out all biological agents would be expensive and time-consuming, therefore, use results from the investigation, intelligence, and resources from the FBI to develop a list of probable agents.
- All samples should follow appropriate chain of custody procedures.

II. Clinical Lab "Rule Out Anthrax" – Bacillus species identified in a clinical sample

Situation: Since the Amerithrax incident, clinical laboratories have been called upon to rapidly determine whether a Bacillus species identified in clinical samples could be anthrax. Bacillus species are very common in the environment, so a "rule out anthrax" is not an urgent situation. Some larger laboratories are able to "rule out anthrax" in their laboratory, whereas some smaller labs may wish to have UPHL perform the testing. Occasionally, this information may be made public or provided to the media, so health department knowledge of the situation is critical to providing rapid, accurate responses. Minimal investigation of these situations is warranted.

- Ensure that UPHL, UDOH epidemiology, and local health department know that a "rule out anthrax" sample is being investigated. The FBI does not need to be notified at this point on a routine "rule out" sample. Use the 1-888-EPI-UTAH number for all UDOH notifications. The on-call epidemiologist should notify the CDEP Program Manager and post the occurrence to the Epidemiology Issue Tracker.

- The culture isolate may need to be transported to UPHL as soon as possible. It should be packaged according to IATA regulations (please see http://health.utah.gov/els/microbiology/btsampletransport.pdf for information on packaging and shipping; follow the guidelines for infectious substances). If a health care facility's courier service will be transporting the isolates, UPHL should obtain relevant contact information and estimated arrival time information from the facility. (UPHL training for clinical labs should stress the importance of speed in ruling out anthrax in a timely manner.)
- The Local Health Department (or UDOH Epidemiology, if requested) should contact the patient's physician to brief them that a Bacillus species was found and that it is routine for these samples to undergo "rule out" testing for anthrax. The physician could be asked if there were any reason to believe that the sample might be anthrax
- UPHL may perform several tests on the isolate to "rule out" anthrax. These tests include:
    - Colony morphology (if colony morphology is incorrect, the lab may elect to terminate further testing)
    - Gram stain
    - Gamma phage
    - DFA (Direct Fluorescent Antibody)
    - PCR (Polymerase Chain Reaction)
    - TRF (Time Resolved Fluorescence)

  These tests will be run concurrently and can take up to 24 hours to complete initial testing. If the testing for all parameters is negative, UPHL will notify the health care facility, UDOH epidemiology, and the Local Health Department. Whatever entity contacted the physician in the previous step should call them to let them know the results of the testing.
- If ANY of the tests are positive or inconclusive the following events should occur:
    - Notify UDOH epidemiology
    - Notify the Local Health Department
    - Notify the FBI
    - Notify the CDC

  Preparations for further investigation should occur at this time. The Local Health Department should initiate their investigation in conjunction with UDOH epidemiology.
- UPHL will perform testing as stipulated by the CDC (Laboratory Response Network) to determine whether a specimen is anthrax.

III. Lab researcher exposure – Known exposure to anthrax

Situation: A physician reports seeing a patient that had a laboratory exposure to anthrax. The patient is either asymptomatic or minimally symptomatic. The physician would like to know what to do.

- Fortunately, anthrax is not transmitted by person-to-person methods so the first point is to educate that this does not present a health threat to the clinical staff.
- Ensure that UPHL, UDOH epidemiology, and the LHD have been notified of this event. Use the 1-888-EPI-UTAH number to contact UDOH. The on-call epidemiologist should assure that the State Epidemiologist, the CDEP Program Manager, the Anthrax Epidemiologist, the State Laboratory Director, the Microbiology Bureau Director, the ELS Division Director, the Local Health Department (including the Local Health Officer) and the FBI are notified. This incident will be posted to the Epidemiology Issue Tracker as well as to UNIS.
- The LHD should initiate an investigation with the University/Laboratory and obtain the following information (UDOH Epi will do this if the LHD requests it):
    - Verify the patient's identity, and the laboratory where they work .
    - Is patient vaccinated against anthrax?
    - What are the circumstances of the exposure:
        - What quantities of organisms were used?
        - What substance was the organism in (ie: powdered spores, liquid vegetative cells, etc.)?
        - What protective devices were being used at the time of exposure (ie: respirators, bio safety cabinets, gloves, etc.)?
        - When was the exposure?
        - Was the exposure reported to safety officers?
- Using the Laboratory Testing portion of this document, public health should assure that appropriate samples are collected and sent to a sentinel or public health laboratory.
- Following the investigation, and working jointly, the UDOH and LHD will determine whether prophylactic antibiotics should be recommended.
- Current prophylactic treatment regimens include the use of ciprofloxacin or doxycycline for 60 days and a 3-dose regimen (0, 2 weeks, 4 weeks) of anthrax vaccine (BioThrax™).

IV. X-ray with "widened mediastinum" or "necrotic skin lesion" – Anthrax in clinical differential diagnosis

Situation: A patient without risk factors presents to a physician with results that are consistent with inhalational anthrax.

- Ensure notification of the UPHL, UDOH epidemiology, and/or the local health department. The local health department will lead the appropriate investigation in conjunction with the UDOH (unless they request that the UDOH lead the investigation). The information should come through the 1-888-EPI-UTAH phone number. The on-call epidemiologist should assure that the State Epidemiologist, the CDEP Program Manager, the Anthrax Epidemiologist, the State Laboratory Director, the Microbiology Bureau Director, the ELS Division Director, the Local Health Department (including the Local Health Officer) and the FBI are notified.

- This event should be posted to Epidemiology Issue Tracker and UNIS.
- Information regarding exposure history and risk factors should be collected as soon as possible to determine if this could be related to a bioterrorism threat. Information should be shared with the FBI as quickly as possible.
- Questions should include:
  1. How many cases have there been? Is the number larger than expected?
  2. Did the person have an appropriate exposure?
  3. Is the age/sex appropriate for this disease?
  4. Is there any geographic clustering apparent?
  5. Has Agriculture been called to see if there is any concurrent outbreak in animals?
  6. Is the antibiotic resistance profile "normal-appearing"?
  7. Are the symptoms (disease presentation) usual?
  8. Was the patient previously healthy?
  9. Have there been unexplained disease, syndromes, or death recently?
  10. Is the time of year appropriate?
  11. Did the patient die?
  12. Did the patient respond typically to therapy?
  13. Does the patient have any other coexisting diseases?
  14. Has surveillance been initiated to determine if similar syndromes (undiagnosed) have been seen?
  15. Is there likelihood that the disease was transmitted via aerosols, person-to-person contact, food, or water?
  16. If more than one person is ill, is there a common ventilation system?
  17. What are the symptoms?
  18. Is the patient a healthcare worker?
  19. Is the patient a laboratory worker?
- Obtain detailed signs/symptoms of the patient.
- Follow the Laboratory Testing area of this protocol to assure that the correct specimens are obtained and sent to a sentinel or public health laboratory.
- Treatment
  - Current treatment consists of ciprofloxacin, doxycycline, or penicillin, see protocols at: MMWR, 10/26/2001; 50(42), 909-919.